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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/057,839 | 01/25/2002 | Samuel Zalipsky | 55325.8167.US04 | 1653 |

22918 7590 10/18/2004

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EXAMINER

KISHORE, GOLLAMUDI S

| ART UNIT | PAPER NUMBER |
|----------|--------------|
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1615

DATE MAILED: 10/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/057,839

Applicant(s)

ZALIPSKY ET AL.

Examiner

Gollamudi S Kishore, Ph.D

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 June 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,2,7-12 and 15 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,7-12 and 15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 6-14-04 & 7-14-04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

RCE filed on 6-14-04 is acknowledged.

Claims included in the prosecution are 1-2, 7-12 and 15.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claims 1-2, 7-12 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0 317 956 of record in view of Waalkes (selective Cancer Therapeutics, vol. 6, #. 1, pp. 15-22, 1990), Diaz et al (Bioconjugate Chem, 1998) also of record.

EP discloses disulfide benzylcarbamate derivatives of anti-tumor drugs.

According to EP, enhanced levels of reducing agents such as NADH, NADPH and glutathione have been associated with human tumor cell lines. These reducing agents act on the disulfide containing prodrugs and thus releasing the drug in the tumor tissue. The drug in EP is bonded to the carbonate group in the benzene ring and the disulfide portion of the compound according to EP is attached to a 'organic functional group that is compatible with the disulfide linkage and the drug moiety' (abstract; page 2, lines 25-31; page 3, line 4 through line 29; page 3, line 44 through page 4, line 10 and pages 8-9). What is lacking in EP is the teaching that the

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organic functional group that is compatible with the disulfide linkage and the drug moiety is a phospholipid.

Waalkes et al teach that intracellular drug retention is higher when the drug is attached to the lipid in the liposome bilayer (abstract and discussion section).

Diaz et al while disclosing generation of phosphatidylserine antibodies teaches the feasibility of attaching the phospholipid to the disulfide moiety (abstract, Figure 1 and Table 1).

It would have been obvious to one of ordinary skill in the art to use phospholipid as the organic functional group in the disulfide containing compound of EP because phospholipids are capable of forming liposomes which are art well-known drug carriers for enhanced drug retention as shown by Waalkes et al. One of ordinary skill in the art would be motivated further to use phospholipid as the organic functional group in the disulfide containing compound of EP because the feasibility of attaching the phospholipid to a disulfide moiety is evident from the teachings of Diaz et al.

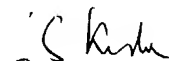
The reference of Asai, which shows increased anti-tumor activity of liposomal phospholipid prodrug, is cited of interest.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK